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Title: Microencapsulation of Vitamins in Food Applications to Prevent  
Losses in Processing and Storage: A Review

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**Abstract:** The food consumption trends have long since shifted from demanding simple calories and essential nutrients in order to support the basic human body functions to demanding a balanced nutrition supply in order to achieve optimal health. Vitamins play a vital role in human health, yet are often lost or destroyed during food processing before they reach consumers, as they are highly prone to degradation by environmental factors. Microencapsulation technology is a technology aiming to protect sensitive compounds from environmental elements. It is widely used in pharmaceutical and cosmetic industries but its application in food production are few. This article reviews microencapsulation studies conducted in food with a specific focus on protecting vitamins from processing and stage losses. We found that although current technologies have the potential to create vitamin microcapsules, none could meet all the criteria for a successful product. To develop suitable vitamin microcapsules which are processing stable, digestible and safe to consume, we recommend further studies to focus on seeking and developing porous and thermal stable carbohydrate or protein based wall materials derived from natural food ingredients.

- Principles of microencapsulation technologies, selection of wall materials, and release mechanisms are reviewed.
- The impact of environmental factors on vitamin stability are complicated and not as established as commonly believed.
- Existing technologies cannot produce vitamin microcapsules that are processing stable, digestible and safe to consume, mainly due to the lack of thermal stable wall materials that are digestible.
- Further studies should focus on developing thermal stable carbohydrate or protein based wall materials derived from natural food ingredients.

1     **Introduction**

2     ‘Vitamins’ are defined as a group of micronutrients that cannot be synthesised by a human  
3     body (Ottaway, 1993). Thirteen identified compounds are further classified into fat-soluble  
4     (A, D, E and K) and water-soluble vitamins (B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, B<sub>5</sub>, B<sub>6</sub>, B<sub>7</sub>, B<sub>9</sub>, B<sub>12</sub> and C). Vitamins  
5     play vital roles in human life with their specific functions to regulate metabolic and cellular  
6     functions, promote health, reproduction and growth, and prevent diseases (Lešková et al.,  
7     2006). Deficiency of vitamins can lead to severe diseases, such as scurvy, beriberi and night  
8     blindness. To ensure the optimal intake of vitamins for the total population, more than 60  
9     countries around the world have implemented fortification plans to fortify staple foods with  
10    vitamins (Teleki, Hitzfeld, & Eggersdorfer, 2013). In 2006, the World Health Organization  
11    (WHO) and Food and Agriculture Organization (FAO) published micronutrient fortification  
12    guidelines to ensure the best practice in fortification plans (Allen, de Benoist, Dary, &  
13    Hurrell, 2006).

14    Vitamins are chemically reactive compounds. During food processing and storage, the  
15    stability of many vitamins is affected by chemical and physical factors such as light,  
16    temperature, pH and oxygen levels (Gregory, 2008), leading to significant nutrient losses in  
17    the end products such as canned products (Rickman, Barrett, & Bruhn, 2007). To prevent  
18    these losses, food industries aspire to seek methods that can protect vitamins in production  
19    and storage. Microencapsulation is a modern technology which integrates bioactive  
20    substances (vitamins, enzyme, phenols, molecules, cells) in the specific coating in order to  
21    protect them from the environmental elements. The process of encapsulating can be carried  
22    out in gases, liquid droplets or small solid particle form in micro sized (1-1000 µm) coatings  
23    (Nazzaro, Orlando, Fratianni, & Coppola, 2012).

24    Microencapsulation is a widely explored subject in many fields. In food, most current studies  
25    are focusing on bioactive compounds such as antioxidants, antimicrobial compounds and  
26    bacteria. In this work, we aim to review technologies that can be scaled up easily and discuss  
27    the possibility of utilising them to produce processing stable vitamins in order to create long  
28    shelf life products with better nutritional values.

## Microencapsulation

Microencapsulation is a process of encasing micron-sized materials in a polymeric shell. The material to be encapsulated may be referred to as the internal phase, core material, fill, payload phase or active agent, whilst the encapsulating material may be referred to as membrane, carrier material, coating, shell, matrix, external phase or wall material (Zuidam & Shimoni, 2010). The microcapsule implies core-wall structure and can be categorised as reservoir and matrix systems. In the reservoir, the core is coated with the wall material, whilst in a matrix system, the core material is embedded within a continuous network of the matrix material lacking a distinctive external wall (Augustin & Hemar, 2009; Singh, Hemant, Ram, & Shivakumar, 2010). The applied pressure can lead to the breakage of the reservoir capsules and hence, the release of its contents. In a matrix type, the active agent is dispersed over the carrier material either in the form of small droplets or more homogenously (Zuidam & Shimoni, 2010). The capsules can be mononuclear where one core material is encapsulated by a shell, or can be aggregated where a capsule consists of multiple-cores (Nazzaro et al., 2012) or can be multi-layered (Augustin & Hemar, 2009). The capsules can be spherical, cylindrical, oval, and irregular shaped (Zuidam & Shimoni, 2010).

The study and application of microencapsulation initially started in the 1930s to make carbonless copy papers (Fanger, 1974). Since then it was extensively employed in many industrial applications including pharmaceuticals, cosmetics and textiles, its application in the food industry has been recognised relatively recently. Microencapsulation is considered a costly process; hence the requirement must be established primarily (Poncelet, 2006). Microencapsulation in food aims to preserve valuable and sensitive components by protecting them from adverse environmental conditions, to prolong shelf-life and to ensure delivery of the encapsulated material to the target location at the desired time (Augustin & Hemar, 2009; Sobel, Versic, & Gaonkar, 2014). For example, protection of polyunsaturated fatty acids and vitamins from oxidation, and protection of probiotics in gastric transit (Poncelet, 2006). Moreover, microencapsulation has the potential to protect sensitive compounds, preserve desirable flavours and aromas or mask unpleasant appearance (Huang, Yu, & Ru, 2010).

Microencapsulating technique can facilitate the convenient handling of materials by allowing the conversion of a liquid food material into a solid or free-flowing powder (Sobel et al., 2014) or vice versa (Huang et al., 2010). An additional benefit of microencapsulation is to

provide a suitable concentration and consistent dispersion of the core material. These functionalities have been widely exploited in drug and vaccine delivery in the pharmaceutical sectors and are increasingly being used to add value to novel food products in the food industry (Olive Li, Dueik González, & Diosady, 2014).

## **Wall materials**

A careful selection of wall material is vital as it imposes the encapsulation efficiency and stability of the microcapsule. The most appropriate encapsulate material for food applications should have the following properties: not reactive with the core, able to seal and retain the core intact inside the capsule, able to effectively protect the core against adverse environmental conditions, lack any unpleasant taste, edible and non-toxic, and economically viable (McClements, Decker, & Weiss, 2007; Nazzaro et al., 2012).

Generally, the ideal wall material should have non-compatible physical properties to the core, such as hydrophobic wall material and hydrophilic core or vice-a-versa. Table 1 summarises the widely used wall materials in food. The properties of these wall materials were reviewed in details by Wandrey, Bartkowiak, and Harding (2010) and Sobel et al. (2014), and updated more recently by Javier D. Hoyos-Leyva, Bello-Pérez, Alvarez-Ramirez, and Garcia (2018) on modified starch wall materials and by Reineccius (2019) on protein wall materials. Attempts at using combinations of wall materials were carried out with various levels of success (Santana, Cano-Higuaita, de Oliveira, & Telis, 2016; Tontul & Topuz, 2013). There is a noticeable gap in the area of utilising microbial protein and lipids as wall material. Microbial proteins have been gradually recognised as a good supplement to the current protein supply (Matassa, Boon, Pikaar, & Verstraete, 2016), which is contributed to by the growth of the meat-free market (Parkes, 2018). Microbial lipids have been suggested as alternative food sources (Bharathiraja, Sridharan, Sowmya, Yuvaraj, & Praveenkumar, 2017) as well as a source for essential fatty acids (Bélignon, Christophe, Fontanille, & Larroche, 2016). Both could be potential wall materials for microencapsulation in food.

## **Microencapsulation Techniques**

Microencapsulation is a multidisciplinary area involving the knowledge and techniques of physics, physical chemistry, polymer chemistry, colloid chemistry, biochemistry, biotechnology, and material science. The methods to prepare microcapsules are broadly divided into two major processes; physical and chemical. A liquid or a gas is normally used



Carter (2004) studied microencapsulation by the spray-drying of multiple emulsions containing carotenoids.

### **Spray chilling/cooling**

In spray chilling, a homogenous mixture of core and molten lipid coating materials are atomised through a sprayer into cooled air below the melting point of the lipid. The cooled or chilled air solidifies the lipid around the core particles. Typically coating materials in spray-cooling would be a lipid or its hydrophobic derivatives with a reasonably high melting point, where a core would be hydrophilic materials such as water-soluble vitamins and enzymes (Kashappa Goud H. Desai & Jin Park, 2005). Some of the food applications are summarised by Favaro-Trindade, Okuro, and Matos Jr (2015). Other studies since then utilised the technique for probiotics (Arslan-Tontul & Erbas, 2017), flavouring agent 2-acetyl-1-pyrroline zinc chloride (2AP-ZnCl<sub>2</sub>) (Yin & Cadwallader, 2018, 2019), and antioxidant proanthocyanidin-rich cinnamon extract (Tulini et al., 2017).

Yet it is possible to use this method to create microcapsules with hydrophobic cores and a hydrophobic wall. A patent (Zoet, Grandia, & Sibeijn, 2012) utilises spray chilling for vitamin D using fat as the wall material, claiming the process is a cheaper alternative to complex coacervation and suitable to be processed at a temperature of 80-90°C for animal feed products. Only two studies were found using the same approach. Paucar et al. (2016) applied the same method on vitamin D<sub>3</sub> and found limited protection of the core at 25°C. Gamboa, Gonçalves, and Grosso (2011) tested the technique on tocopherols and found good retention rate at room temperature, however, the study did not include data for control (unprotected tocopherols).

Another approach is double layered microencapsulation. The hydrophobic core is first coated with a hydrophilic coat using spray drying then coated again with a hydrophobic coat using spray cooling. This approach was tested on fish oil, sachal oil (Fadini et al., 2018) and probiotics (Arslan-Tontul & Erbas, 2017).

### **Coacervation**

Coacervation is defined as the separation of a colloidal solution into two liquid phases (Burwell, 1976). There are two types of coacervation processes: simple and complex. Simple coacervation uses a single polymer to form coacervates through the addition of salt or dissolving agent (Timilsena, Akanbi, Khalid, Adhikari, & Barrow, 2019), the dissolving

agents could be alcohol or acetone (Elzoghby, Elgohary, & Kamel, 2015). Simple coacervation is relatively less studied in food. Kafirin, a sorghum prolamin storage protein, has been used to encapsulate tannins (Links, Taylor, Kruger, & Taylor, 2015). Sutaphanit and Chitprasert (2014) used gluten coacervates for microencapsulation of holy basil essential oil. Hydroxypropyl methylcellulose (HPMC) simple coacervation is used to encapsulate fish oil (Wu & Xiao, 2005).

In complex coacervation, two or more polymer solutions with opposite charges electrostatically interact with each other in water resulting in two immiscible liquid phases: the polymer-rich dense phase and the polymer-poor continuous phase. The former is commonly called coacervate and can be used as a coating for a wide range of core materials. The first investigation on the gelatin-gum arabic system was investigated by Bungenberg de Jong and Kruyt in 1929 (de Kruif, Weinbreck, & de Vries, 2004), which became a primary choice for the food industry (Thies, 2003). The complex coacervation generally involves several steps shown in Figure 1. The core materials are firstly dispensed in a cationic polymer water solution (normally a protein). Then an anionic polymer solution is added (normally a carbohydrate). With the adjustment of pH and temperature, coacervate microdroplets start separating from the continuous polymer phase. When water-insoluble core materials are presented, the coacervate microdroplets form to interact with the core surface and gradually form a continuous shell. A crosslinking agent such as transglutaminase and glutaraldehyde are often used to strengthen the gel. The complex coacervation technique can be applied to many water-insoluble compounds such as fatty acids, fat soluble vitamins and flavours. More detailed applications using complex coacervation in food have been reviewed by Eghbal and Choudhary (2018) and Timilsena et al. (2019).

Although the technique is considered as complex, time-consuming and costly compared to spray drying, it can offer many advantages including: mild temperature changes, high shell integrity, high core loading, maximum encapsulation efficiency, and great controlled-release (Gouin, 2004). Many physicochemical parameters influence the complex coacervation process. Some are environmental such as pH, temperature, pressure, and stirring; others are based on properties of the polymers including molecular weight, ionic strength, concentration, and the protein/polysaccharide ratio. Schmitt and Turgeon (2011) considered pH, ionic strength, protein to polysaccharide ratio and total biopolymer concentration as the most important factors.



## **Extrusion**

The earliest pioneer work using extrusion for encapsulation appeared in the late 1950s in the flavour industry, known as melt injection (Castro et al., 2016). Despite the early discovery, commercial extrusion for the microencapsulation of active agents is a relatively less used process in the food industry (Oxley, 2014). In the extrusion method, a core material is incorporated into molten carbohydrate mass, and then the mixture is forced through a series of dies and collected in a bath of dehydrating solution (Reineccius, 2019). The coating hardens in the bath, then is separated, dried, and sized. Common coating materials used include glucose, glucose syrup, sucrose, maltodextrin, and glycerine, which can be used as a single or a mixture of compounds. The primary advantage of this method is the protection of the core compounds from oxygen as they are completely isolated from the air by the wall material (Gibbs, Kermasha, Alli, & Mulligan, 1999).

Some considered coextrusion as a separate technology to extrusion (Gouin, 2004; Oxley, 2014). From the engineering point of view, coextrusion is a variation of the extrusion technology allowing layered construction of a material (Mount, 2011). In extrusion, a wall material matrix containing cores is formed before being extruded; where in coextrusion, core materials and wall materials are injected through separate pathways to the inner and outer parts of a double fluid nozzle. The combined materials then are extruded through a die and form round beads due to Raleigh instabilities (Gouin, 2004). One of the advantages of coextrusion is the possibilities of producing multi-layered microcapsules.

## **Liposome Entrapment**

Liposome was first discovered by Alec Bangham in 1965 (Bangham, Standish, & Watkins, 1965). Liposomes are vesicles made of bilayer mostly composed of phospholipids, which are formed as a result of dispersion of phospholipids into aqueous solution and exposure to high shear rates through microfluidisation or colloid mill. Phospholipids have amphipathic characteristics, which means they contain both hydrophilic and hydrophobic head groups. The polar end can bind to water-soluble particles, whilst the non-polar end binds to oil-soluble particles. When suspended in an aqueous solution containing water soluble core molecules, the phospholipids form a sheet first as their non-polar ends align with each other, then form a sphere (liposome) with their hydrophilic ends inside the sphere, trapping part of the aqueous solution with the core materials. One advantage of this method is that it allows the core material to maintain high water activity, where the other methods discussed above

deprived water from the core in the process (Mirafzali, Thomas, & Tallua, 2014). This is important for applications requiring high water activity for the core to be active, such as enzymes and probiotics. Phospholipids are abundant membrane lipids which naturally occurred in animal cells, this potentially gave liposome another advantage on biocompatibility. Due to this advantage, liposome became a useful delivery system for drugs (Li et al., 2019). Many studies use liposome to encapsulate nisin, a natural antibacterial compound (Lopes, Barreto Pinilla, & Brandelli, 2019; Niaz et al., 2018). Also cheese is of particular interest in liposome application, as entrapped enzymes can be used to control the ripening process (Kheadr, Vuillemand, & El-Deeb, 2003; Laloy, Vuillemand, Dufour, & Simard, 1998). Liposome could also be used reversely to entrap a fat-suitable material to create more water suitable particles. These methods included thin film hydration, freeze–thaw, rapid expansion of supercritical solution (RESS) and precipitation from gas saturated solution (PGSS), which were reviewed in details by Sherry, Charcosset, Fessi, and Greige-Gerges (2013).

Various factors limit the usage of liposome in the food industry however. The first is stability. As a lipid, phospholipids are prone to oxidation and hydrolysis as well as sensitive to low or high pH and heat, particularly when unsaturated phospholipids are used in order to reduce cost or encapsulate fat-soluble cores by trapping them between the phospholipid molecules (Mirafzali et al., 2014). Typically, this results with the liposomes being required to be stored at chilled temperature (Sebaaly, Jraij, Fessi, Charcosset, & Greige-Gerges, 2015) and it can be difficult for them to survive processing. This however can be improved by incorporating additional coatings such as pectin (Lopes, Pinilla, & Brandelli, 2017).

## **Release Mechanism**

Although the main purpose of microencapsulation is to protect the core materials from environmental elements, it is meaningless if the cores cannot be released or are released at the wrong time or place. Therefore, the release mechanism of the core at the appropriate place and time is as important as the protection capacity for microencapsulation.

The main factor to the release rate is associated with interactions between the carrier and the core materials. Additionally, other factors that influence the core release are the volatility of the core, the ratio of the core and the wall material, particle size, and viscosity of the wall material (Ganza-González, Anguiano-Igea, Otero-Espinar, & Blanco Méndez, 1999).

Controlled release is a strategy to release bioactive agent at the target site, at the target rate and at the target time. The release profile of a microcapsule describes its release triggers and release kinetics. The mechanisms of release are described below, in practice, a combination of more than one mechanism is used. Singh et al. (2010) summarised the mechanisms of microcapsules delivery in drugs into diffusion, dissolution, osmosis and erosion. We consider some of the release triggers such as enzymes, pH and temperature to be individual mechanisms as they can be controlled independently to each other in various delivery situations.

**Diffusion:** occurs especially when the microcapsule shell is intact. Dissolution fluid dissolves the core by penetrating the wall material leading to leakage through the pores or interstitial channels (Gunder, Lippold, & Lippold, 1995). Early work suggested the final release relies on the penetration rate of microcapsule by dissolution fluid, the dissolving rate of the core into the dissolution fluid, and the leakage and dispersion rate of the core (Higuchi, 1963). The core can be released with or without shell swelling (Shahidi & Han, 1993). In practice, the rate of diffusion is also influenced by the type of core material and wall material, the type/size/shape of the microcapsule (Siepmann & Siepmann, 2012).

**Dissolution:** when the coating gradually dissolves, the cores are released. Therefore the release rate is determined by the dissolution rate (Gunder et al., 1995), which is influenced by the thickness of the coating and its solubility in the dissolution fluid. An example of this mechanism is the release of microencapsulated coffee flavours in contact with water, whilst the flavour can be protected from heat, light and oxidation in the dry state (Frascareli, Silva, Tonon, & Hubinger, 2012).

**Osmosis:** the polymer shell of the microcapsule resembles a semi permeable membrane. The osmotic pressure difference between inside and outside of the microcapsule lead to the movement of the core through small pores in the shell (Singh et al., 2010).

**Biodegradation:** in a biodegradation release mechanism, enzymes such as proteases and lipases hydrolyse proteins or lipids, respectively, leading to release of the core. Hickey, Kilcawley, Beresford, and Wilkinson (2007) discovered that enzymatic degradation enhances the ripening of cheddar cheese by 50% faster than the conventional ripening process.

**pH:** the principle of the pH release profile is to alter the solubility of the wall material by changing the pH of the environment. For instance, microencapsulation based on the pH release mechanism enables the release of riboflavin in the intestine where the pH is alkaline, skipping through the acidic pH of the stomach (de Farias et al., 2018).

**Temperature:** alteration in temperature enables core release. This mechanism is based on two concepts: temperature-sensitive release and fusion-activated release. The former is based on the expansion or collapse of the wall material at a critical temperature, whereas the latter one is based on the melting of the wall material when temperature rises (da Silva et al., 2014).

**Pressure:** a release is triggered when pressure is applied to the core material. Releasing flavours from chewing gum during mastication is an example of this mechanism (Wong, Yu, Curran, & Zhou, 2009).

### **Interests and challenges**

Microencapsulation is widely studied and applied in pharmaceuticals and has become a significant interest in the food industry. The technology also found its applications in cosmetic (Martins, Barreiro, Coelho, & Rodrigues, 2014), metal coating (Wazarkar et al., 2016) and textile (Arantzazu, Marina, Ana, & Maria, 2018). For food applications, there are many challenges in developing efficient and suitable microencapsulation systems. In our opinion, the greatest challenge is to find a suitable material and method to create coatings able to survive aggressive food processes. Although many novel processing technologies that are less aggressive are emerging to the food industry, most commonly used technologies still involve a large amount of mechanical operation and heat treatments at high temperature. Most microencapsulation studies only considered the stability of the microcapsules in storage temperatures, where few tested their stability under processing conditions. On the other side of this challenge, a microcapsule is only useful if it can be released at the desired time and location, which is in the human digestion system for most food applications. Therefore, the release mechanism of the microcapsules must be effective. To add to the difficulty, the selection of materials is restricted for food applications as well as they must be suitable for human consumption, and the economic feasibility for large scale production must be considered. Despite these challenges, the high potential of microencapsulation led to a substantial rise of scientific interests in this field. A quick survey using “microencapsulation”

as the keyword for topics on Web of Science shows the number of publications rose from 147 in 1998 to 860 in 2018.

## **Vitamins in food system**

Due to an increase in popularity of functional food, food industries have begun to add vitamins to food and beverages. However, many of the micronutrients including vitamins have limited stability and are highly reactive with many other food compounds. During food processing and storage periods, the stability of many vitamins can be affected by various chemical and physical parameters such as light, temperature, and pH. Moreover, the flavour of vitamins can be strong and even unpleasant, making the food less appealing (Delompré, Guichard, Briand, & Salles, 2019). Suitable microencapsulation methods can contribute to the protection of these sensitive compounds by eliminating or limiting nutrient loss, masking their flavour and appearance, and allowing controlled release of the compounds (Huang et al., 2010)

## **Vitamins and strategies to prevent their deficiency**

In 1912, Casimir Funk discovered ‘vital amine’ which was later known as vitamin (Teleki et al., 2013). The isolation of all 13 major vitamins had been accomplished and their synthesis had begun by the mid-20<sup>th</sup> century (Mozaffarian, Rosenberg, & Uauy, 2018). Vitamins take part in various biochemical functions in the human body, hence they are classed as essential micronutrients. For example, some B-group vitamins perform as coenzymes to provide energy, vitamin C participates in numerous physiological processes, such as the immune response and iron absorption (Bender, 2009). The majority of the vitamins have to be supplied through diet as they cannot be synthesised in the human body with the exception of some amounts of niacin and vitamin D (Drouin, Godin, & Pagé, 2011).

A diet deprived of vitamins can result in various deficiency diseases like pernicious anaemia, pellagra, beriberi, scurvy, dermatitis, ariboflavinosis, enteritis, and many more (Gregory, 2008). Only an insignificant amount of water soluble vitamins, with the exception of vitamin B<sub>6</sub> and B<sub>12</sub>, are stored in the body (Bender, 2009). Fat-soluble vitamins are stored in lipid fractions such as adipose tissues, however, the absorption rate can be poor such as in the case of vitamin E (Barasi, 2003). The micronutrient deficiency is often unnoticed, therefore often termed ‘hidden hunger’. Micronutrient deficiencies are most predominant in developing countries due to their diet lacking variety (Ritchie & Roser, 2020). Many strategies have been

proposed to prevent vitamin deficiencies, broadly speaking, they can be categorised into either supplementation or food-based strategies (Gibson, 2011). Dietary diversification is a food-based strategy encouraging and helping the population to consume more diverse types of food in order to achieve a more balanced diet. It is ideal in theory as there is no modification of the food nor additional risks from taking supplements. However, it requires social and even cultural changes in the community, which can be hindered by economic, social and cultural barriers (Akhtar, Ismail, Atukorala, & Arlappa, 2013; Nyantakyi-Frimpong, 2017).

Supplementation is a direct approach, which has the potential to rapidly correct the micronutrients status in the human body. The supplement industry took this opportunity to market single and multivitamins as a means to protect against their deficiency (Mozaffarian et al., 2018). However, the effectiveness of the vitamin supplement is widely debatable within the science community. Some find they might be effective in a particular case, such as vitamin D on reducing the onset of preeclampsia (Fu, Ma, Liu, Wang, & Guo, 2018) and multivitamin supplementation on reducing the risk of autism spectrum disorder in children (Guo, Li, Zhai, & Ding, 2019). Others argued that they made no difference or even carried higher risks than a balanced diet (Combet & Buckton, 2019; Hamishehkar, Ranjdoost, Asgharian, Mahmoodpoor, & Sanaie, 2016; Jenkins et al., 2018; Tucker, Safadi, & Friedman, 2015). Fortification is a supplementation strategy of adding nutrients to food at levels higher than originally found. This is to either restore micronutrients lost during processing, provide a more nutritionally balanced food than their original form, or provide a special purpose food designed to perform a specific function (Allen et al., 2006). Food fortification has been widely used for many decades and has been considered as one of the most effective public health measures to prevent micronutrient deficiency disorders in developed countries (Teleki et al., 2013). However, the efficiency of vitamin fortification often is not maximised due to the vitamin instability in processing and storage. To overcome this issue, microencapsulation can be a good solution to enhance the effectiveness of the fortification.

### **Vitamin loss in processing and storage**

Vitamins are heterogenous compounds with different chemical and physical properties. A common attribute they share is their instability in food, whether they are occurring naturally or synthetically added (Ottaway, 2010). Various factors can affect the stability of vitamins in

storage (Figure 2). Individual vitamin's response to these factors varies. Several textbooks and reviews provided tables overviewing the stability or sensitivity of vitamins to main environmental factors including light, oxygen, heat, moisture/humidity, and pH. The sources of these tables are mostly from early publications such as Harris (1988) adopted by Gregory (2008). As Gregory rightly advised, the conclusions of these early works are oversimplified. Therefore caution is needed when using these tables. We conducted a mini review using "stability" and "Vitamin A" as keywords, aiming to seek evidence to support the indications in Harris's table. Strong evidence was found supporting light, temperature and oxygen as primary causes of vitamin A loss in storage (Fávaro, Iha, Mazzi, Fávaro, & Bianchi, 2011; Ferguson, Emery, Price-Davies, & Cosslett, 2014; Gupta, Arora, Sharma, & Sharma, 2019; Hemery et al., 2015). Hemery et al. (2018) also found some evidence suggesting higher humidity could also have a negative effect however only when samples were packed in paper bags which has a limited oxygen barrier capacity, but not in PET/aluminium bags. We were able to find only one study which directly addressed the effect of pH on vitamin A stability. Carlotti, Rossatto, Gallarate, Trotta, and Debernardi (2004) tested the stability of retinyl palmitate in hydroxy ethyl cellulose hydrogels under UV light and found natural pH (from 5.6 to 7.0) had no impact on retinyl palmitate's photostability, however, lower and higher pH (4.0 and 8.0) decreased the photostability of retinyl palmitate, which is contrary to Harris' indication that vitamin A is stable in an alkaline environment. There are also other factors not presented on the table such as the presence of fat/lipid and the type of fat/lipid could impact the stability of vitamin A. Lau, Kakuda, and Arnott (1986) and Moccand et al. (2016) both found fat/lipid has a protective effect on vitamin A against degradation, and Moccand et al. (2016) found a more saturated fat/lipid has a stronger protective effect. This mini exercise demonstrated that the environmental influences on vitamin stability are complicated and understudied despite vitamins having been discovered for over 100 years.

Loss of vitamins occurring during cooking processes have been reported in many early food and nutrition studies. Ascorbic acid and thiamine in vegetables and fruits are the most susceptible vitamins to degradation during cooking (Harris, 1988). Scott and Bishop (1986) found pasteurisation resulted in a 25% loss of vitamin C in raw milk, which increased to 30% and up to 60% during UHT and sterilisation respectively. Blanching is a common pre-process step used to alter the properties of raw materials before main processes such as baking, frying and canning. Sungpuag, Tangchitpianvit, Chittchang, and Wasantwisut (1999) reported

blanching of vegetables caused 7-11% loss of retinol, while boiling resulted in the highest loss of 43% in cooked traditional Thai food.

Regardless of whether freezing is considered as a processing step or storage step, the loss of nutrients in freezing and thawing is well established. Loss of thiamine in meat and ascorbic acid in fruits and vegetables were found to be directly proportional to the frozen storage time (Kramer, 1977). Adams and Erdman (1988) reported significant vitamin leaches during thawing. Although most of the vitamins are chemically stable in frozen fruits and vegetables for periods of up to a year, losses of vitamin C have been found to occur at temperatures as low as -23°C (Ottaway, 2010). Refrigeration is regarded as a good storage method for retaining nutrients in food because no ice crystallisation occurs and there are limited chemical/biological changes due to the relatively low temperature. However the chilled temperature combined with unsuitable humidity still can result in wilting of fruits and vegetables, which lead to the loss of vitamins (Severi, Bedogni, Manzieri, Poli, & Battistini, 1997).

Several modern commercial nutrition databases such as “SELF Nutrition Data” includes information on nutrition retention or loss in processes. Most of these are based on a dataset from the NLG project carried out in Europe (Nutrient Losses and Gains in the preparation of foods project 1983-1993) (Bergström, 1994) or USDA Table of Nutrient Retention Factors produced by United States Department of Agriculture (USDA) (Nutrient Data Lab, 2017). Both datasets are available for the public.

## **Microencapsulation application for vitamins**

### **Previous studies**

Microencapsulation is relatively new in the food industry, and much of the research is focussed on flavours and colouring. A few reviews have been published on individual vitamins including vitamin A (Gonçalves, Estevinho, & Rocha, 2016; Loveday & Singh, 2008) and vitamin C (Abbas, Da Wei, Hayat, & Xiaoming, 2012). Perhaps it is because Vitamin C is known as one of the most perishable vitamins in processing and storage, whilst vitamin A is widely used in food and beverage formulation as a colouring, an antioxidant or a nutrient. Table 2 summarises encapsulation methods and wall material used, product particle size and their release and retention behaviour from recent studies on vitamins for food applications.



In the last decade, very few coating materials were known to be of food grade standard. With the requirement in mind that, to protect the vitamins in food products, the delivery system must be derived from permitted food ingredients via regulated food processing systems. Recently, more studies in edible coating materials have been seen, particularly abundances in the field of hydrocolloids. The potential of using taro starch to encapsulate ascorbic acid was tested by J. D. Hoyos-Leyva, Chavez-Salazar, Castellanos-Galeano, Bello-Perez, and Alvarez-Ramirez (2018). Although only limited encapsulation efficiency was achieved (20.9%, whereas it is normally in the range of 50-60% for this technique), higher stability at high humidity and temperature during the storage period was reported. Food protein-based carriers for vitamin and other bioactive delivery have also been reported and reviewed (L. Chen, Remondetto, & Subirade, 2006; Egan, Jacquier, Rosenberg, & Rosenberg, 2013; Livney, 2010). Combinations of alginate and pectin (alg-pec) polymers were reported as a suitable carrier for Folic Acid (FA) (Alborzi, Lim, & Kakuda, 2013; Madziva, Kailasapathy, & Phillips, 2005, 2006; Shrestha, Arcot, & Yuliani, 2012).

Liposomes delivery system has been on the rise in the latest decades (Gouin, 2004), the system has been used to deliver enzymes, proteins, flavours, antioxidants, and vitamins. Several studies have been reported on the use of liposomes to stabilise vitamins including ascorbic acid (Jiao, Wang, Yin, Xia, & Mei, 2018; Marsanasco, Márquez, Wagner, del V. Alonso, & Chiaramoni, 2011; Wechtersbach, Poklar Ulrih, & Cigić, 2012), retinol (S. C. Lee, Lee, Kim, & Lim, 2005; S. C. Lee et al., 2002) and  $\alpha$ -tocopherol (Marsanasco et al., 2011). Most liposome bilayers are formed by soy phosphatidylcholine (PC), but ascorbic acid and pantothenic acid have been coated in dipalmitoyl-phosphatidylcholine (DPPC) (Wechtersbach et al., 2012) and phospholipon 90 G (Ota et al., 2018). Retinol incorporated into PC liposomes at 0.01:1- 0.05:1 retinol to PC ratios, showed almost 100% encapsulation efficiency and improved stability under all conditions. In the alkaline buffer, 90% of retinol was retained after 8 days of storage whereas only about 10% of free retinol was remaining after 1 day (S. C. Lee et al., 2002). Effects of cholesterol (CH) addition in liposomes have also been studied in vitamins. S. C. Lee et al. (2005) added CH to PC at various ratios into the formation of liposomes and found CH increased the encapsulation efficiency and stability. Wechtersbach et al. (2012) used DPPC with CH to form liposomes capsules of ascorbic acid. They found half-lives of ascorbic acid were increased 300 fold along with improved thermostability even during high temperature and low time pasteurisation (72°C).

Ota et al. (2018) stabilised pantothenic acid by capturing the vitamin into liposomes then extruding with polysaccharide polymers (sodium alginate and pectin) and found improved stability. After 14 days of storage, only 20% release occurred at pH 4 and improved thermostability was also reported.

Solid lipid nanoparticles (SLN) as a drug and cosmetic delivery system have been a growing trend. SLNs are submicron-sized lipid emulsions consisting of solid lipid instead of liquid lipids (Mukherjee, Ray, & Thakur, 2009). This system has several advantages when considering food production, including being easily scalable, can be made without using solvents and great biocompatibility (Aditya & Ko, 2015). An obvious limitation of SLN is its suitability for encapsulating hydrophilic cores. There are very few studies which encapsulate vitamins in SLN for food application. Salminen, Gömmel, Leuenberger, and Weiss (2016) encapsulated vitamin A and  $\beta$ -carotene in SLNs made from Tristearin using *Quillaja saponaria* extract and lecithin as an emulsifier. They found the oxidative stability differed significantly between the two cores. The oxidative stability of unprotected cores was not tested, therefore, the protective effect of the SLN was not concluded in that study. Similarly, Mehrad, Ravanfar, Licker, Regenstein, and Abbaspourrad (2018) also entrapped  $\beta$ -carotene, but in SLN composed of palmitic acid and corn oil. They have found improved chemical stability via measurement of the loss of colour intensity.

In recent years, some studies reported on the use of nanomaterial coating such as gated mesoporous silica particle (MSP). Pérez-Esteve et al. (2015) proposed an MSP delivery system to encapsulate FA and reported enhanced stability and *in vitro* target release of the system. Ruiz-Rico et al. (2017) used the delivery system in fortification of fruit juice with MSP-FA microcapsule. Only 10% of FA was released in the juice over the testing period at pH 3.5, however, most of FA were released at pH 7.5 in less than two hours. This indicates the significant potential of MSP as a smart delivery system which can protect vitamins from an acidity environment in the stomach while allowing nutrient release in the small intestine which has a near natural pH of 6 (Fallingborg, 1999). Many may consider MSP and other nanosilica potentially harmful, most likely linked to silicosis, a lung disease caused by exposure to crystalline silica dust (Leung, Yu, & Chen, 2012). However the adverse health effects of nanosilica are still unclear and under further investigation (Murugadoss et al., 2017).

A delivery system that has similar release behaviours to MSP but is based on natural edible ingredients was found by Ahmad, Qureshi, Maqsood, Gani, and Masoodi (2017). They used horse chestnut starch (HCS) and  $\beta$ -cyclodextrin as wall materials to entrap FA using spray drying. Although the encapsulation yields were still less than 60%, it indicated the potential of developing a smart delivery system using natural edible ingredients.

Nanoencapsulation is an emerging technology (Gouin, 2004) aiming to produce smaller particle size compared to the traditional microencapsulation. Nanoemulsion has been frequently used, particularly in the formation of liposomes (Jiao et al., 2018; Ota et al., 2018; Wechtersbach et al., 2012). The nanoemulsion process was also employed in MSP delivery systems (Pérez-Esteve et al., 2015; Ruiz-Rico et al., 2017) and electrospinning (Alborzi et al., 2013) to encapsulate FA, in spray drying for vitamin D (Moeller, Martin, Schrader, Hoffmann, & Lorenzen, 2018) and  $\beta$ -carotene (Liang, Huang, Ma, Shoemaker, & Zhong, 2013), and in emulsion encapsulation of vitamin E (C. C. Chen & Wagner, 2004). Higher encapsulation efficiencies and vitamin stabilities were reported in all cases. The benefit of nanoemulsion is increased stability of emulsion due to the smaller droplet size (Jafari, Assadpoor, Bhandari, & He, 2008).

Lešková et al. (2006) stated that retinol, folate, thiamine and vitamin C are the most unstable vitamins during processing, with retention below 40%. In contrast to the abundant attempt to encapsulate the other three vitamins, we found only one study on encapsulation of thiamine in food. Juveriya Fathima, Fathima, Abhishek, and Khanum (2016) used phosphatidylcholine as the wall material to create nanocapsules of thiamine and found good encapsulation efficiency, however the retention in storage was not tested, and chloroform was used in the process therefore it is not suitable for human consumption. There is also a lack of similar studies on biotin, pantothenic acid, B<sub>12</sub>, riboflavin, vitamin D, and Vitamin K. This might be led by considerations that these vitamins are relatively stable (Lešková et al., 2006) therefore no further protections are needed. However, as we have demonstrated above using vitamin A as an example as well as discussed by Lešková et al., the stability/sensitivity of many vitamins are understudied and not fully understood. Therefore, further work in that area and subsequently potential encapsulation studies are needed. Also, protection from environmental factors is only one useful aspect of microencapsulation. There could be many other applications focusing on processing functionality such as coating a water soluble vitamin with a hydrophobic coating in order to incorporate it better in fat rich food.

## Select suitable wall materials

In order to discuss more effectively in this section, we set the following criteria for a wall material that would be suitable to produce processing stable vitamin microcapsules:

- Able to protect cores from environmental elements in food processing including high temperature, pressure, mechanical stresses, oxygen, acidity and alkaline, moisture, and other reactive compounds
- Digestible in the human digestive system
- Safe for human consumption, ideally derived from natural edible ingredients
- Ideally odourless and colourless
- Good solubility in water
- Inexpensive

Carbohydrates, or specifically, polysaccharides are good candidates for wall materials, considering their capability of forming larger porous molecular structures (L. Liu, Shen, Zhang, Li, & Zhu, 2018), they are mostly from natural food ingredients and widely used in food industry, and many of them are digestible in the human digestion system. Fathi, Donsi, and McClements (2018) reviewed carbohydrate based microencapsulation systems and found a variety of potential applications including increased acid resistance, increased solubility in natural pH, and increased heat resistance. However, none of the attempts reviewed could satisfy the criteria discussed above. Proteins, similarly to carbohydrates, are good candidates. Fathi et al. (2018) summarised the physicochemical properties of proteins that were used as wall materials for food ingredients. Collagen, gelatin and casein were suggested as having high-temperature stability, where gelatin and casein also have good solubility in water. However, there is a lack of experiment data to prove these concepts. For lipid based encapsulations, methods like SLN are useful for improving storage stability of fat soluble vitamins, however, they are not suitable for products requiring further thermal processing as the solid fat coats will melt and therefore lose their protective properties. On the other hand, liposome entrapment could be used as an initial coating method to improve water solubility of fat soluble vitamins (Sherry et al., 2013), subsequently enabling them to be encapsulated in a hydrophilic coating.

## Suitable encapsulation techniques

Similar to the selection of wall materials, general criteria should be set when selecting techniques for vitamin microencapsulation: a) avoid heat, mechanical stress, and oxygen, b) safe for food production, c) scalable, d) inexpensive to operate. Different applications would also require individual criteria such as the physical format of the end product, particle size/structure/morphology and solubility in water/oil. For an application to incorporate vitamins in thermal processed food such as cans a selection of suitable techniques is critical as they are susceptible to many elements commonly occur in processes, particularly heat (Bergström, 1994). Yet low temperature techniques, including spray cooling and liposome entrapment, were most used when lipids/fats are wall materials which will lose their protective properties when heated. Therefore, none-thermal techniques would be most suitable for this application. Vacuum spray drying limited the heating and oxygen in the process, it has been successful utilised to produce highly viable dry probiotics (Semyonov, Ramon, & Shimoni, 2011) and bovine serum albumin microcapsules (Freitas, Merkle, & Gander, 2004). Super critical fluid, particularly super critical carbon dioxide, technologies have been widely used in pharmaceutical microencapsulation application (Soh & Lee, 2019). It has been used to encapsulate  $\beta$ -carotene (de Paz, Martín, & Cocero, 2012; de Paz, Martín, Duarte, & Cocero, 2012), vitamin B2 (Couto, Alvarez, & Temelli, 2017) and vitamin E (Prieto & Calvo, 2017). Although these studies were not designed to produce processing-stable products, the many unique properties of super critical CO<sub>2</sub> allow it to act as a solvent, anti-solvent, solute, drying medium, and foaming agent in the microencapsulation process (Soh & Lee, 2019), which provides many possibilities for designing a suitable process. Membrane emulsification is a relatively new technique for producing a range of products from simple oil-in-water (O/W) and water-in-oil (W/O) emulsions to complex microcapsules (Vladislavljević & Williams, 2005). The general principle of membrane emulsification is to force the dispersed phase through a porous membrane into a moving continuous phase (Laouini, Fessi, & Charcosset, 2012; Wang et al., 2020). A variation of this technique is to pre-mix the dispersed phase and continuous phase, then focus the mixture through a porous membrane (Eisinaite, Juraite, Schroën, & Leskauskaitė, 2016). It is characterised by its low energy consumption, good control of droplet size distribution, and overall mildness of the process (Laouini et al., 2012). Membrane emulsification has been used for various food applications including encapsulation of polyphenols (Wang et al., 2020), vitamin E (Laouini

et al., 2012) and vitamin B12 (Matos, Gutiérrez, Iglesias, Coca, & Pazos, 2015). Another advantage of membrane emulsification is that it has good scalability (Piacentini, Giorno, Dragosavac, Vladislavljević, & Holdich, 2013) and industrial solutions are already available from companies such as Micropore, UK.

## Design of future study

One of the difficulties we experienced in this review work is that many studies did not provide a full set of information in order to determine the efficiency of the tested wall material/delivery system. For the purpose of producing a processing stable vitamin microcapsule for food applications, the system needs to provide information on: a) encapsulation efficiency; b) vitamin retention under various food processing conditions, for example, retention after a F6 sterilisation process; c) validation of retention in food applications; d) release rate in an environment similar to the human gastrointestinal tract. If the microcapsules were produced using food safe materials and procedures, organoleptic properties should also be tested. The aim of an encapsulation efficiency test is to determine the quantity of the vitamin molecules captured by the encapsulation process. Test methods can be designed based on differences of the physiochemical properties between the microcapsule and the vitamin. For example, this could be solubility differences in water (K. G. H. Desai & Park, 2005) or solubility differences in solvents (Romo-Hualde, Yetano-Cunchillos, González-Ferrero, Sáiz-Abajo, & González-Navarro, 2012). Many studies we have seen did not include release rate data, and very few were tested in an environment similar to the human digestion system. A standardised static *in vitro* digestion module has been established by (Minekus et al., 2014) and been used in many food digestibility studies (T. Liu et al., 2016; Smith et al., 2015). It is fairly easy to set up and does not require specialised equipment such as a Dynamic Gastrointestinal Simulator (DGS). However, the information it can provide is invaluable as only the released vitamins are available for absorption and meaningful for health.

## Conclusion

Vitamins are essential for human health, and their deficiency can lead to several diseases. Fortification is an important strategy to battle vitamin deficiency, however, many of the vitamins are susceptible to degradation in food processing. Microencapsulation can improve their stability, help them survive food processes and storage and ensure they are released in a

suitable part of the human digestion system in order to provide maximum benefits. The stability/sensitivity of many vitamins is understudied and not fully understood. This hinders the research interests in encapsulation of some vitamins which are traditionally considered as stable. To achieve the optimal encapsulation efficiency and retention of the vitamin, it is essential to select appropriate wall materials and methods based on the chemical and physical properties of the vitamins to be encapsulated. Wall material properties and processing conditions dictate the morphology, particle size and final characteristics of the encapsulated vitamins. Seeking digestible wall materials which can also protect vitamin cores from food processing elements is critical for creating long shelf life food products with fortified vitamins.

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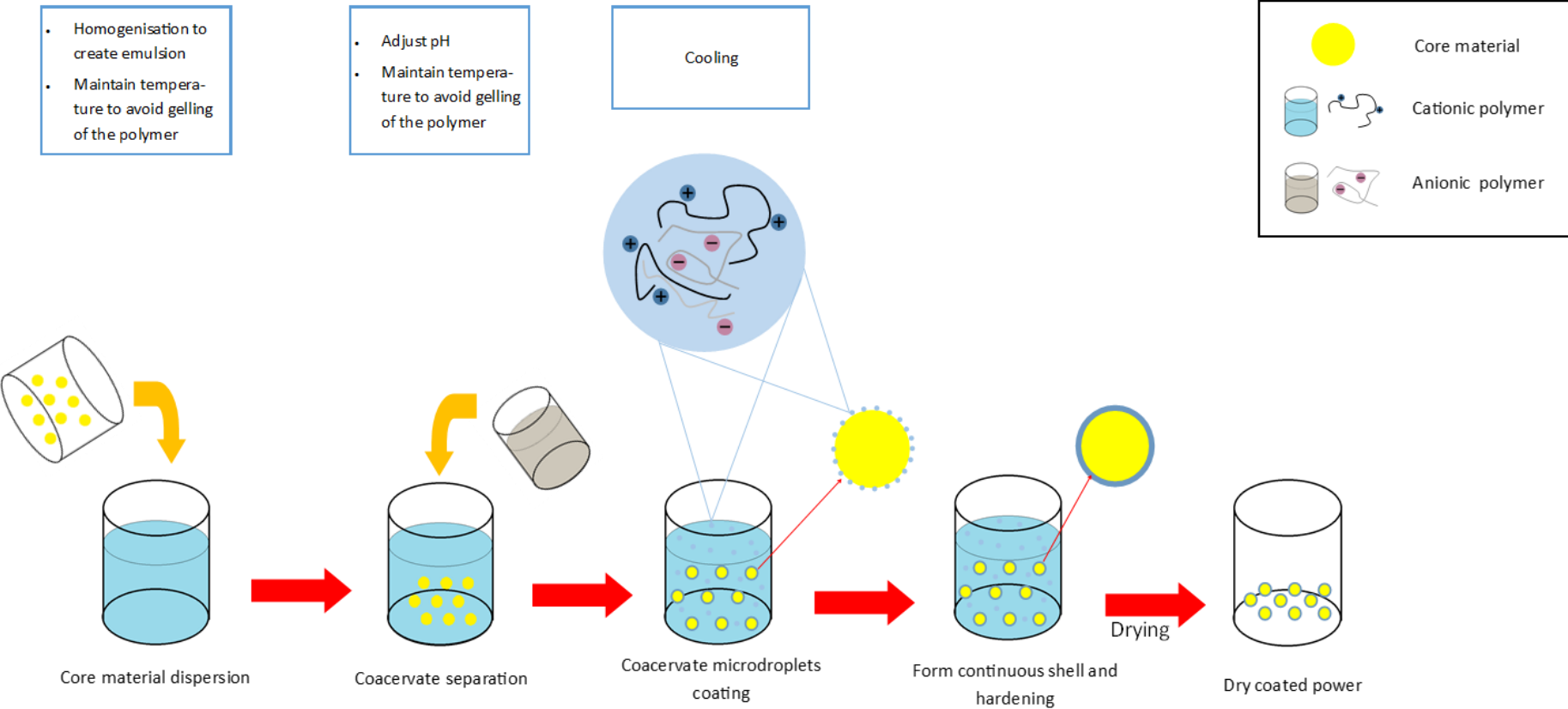


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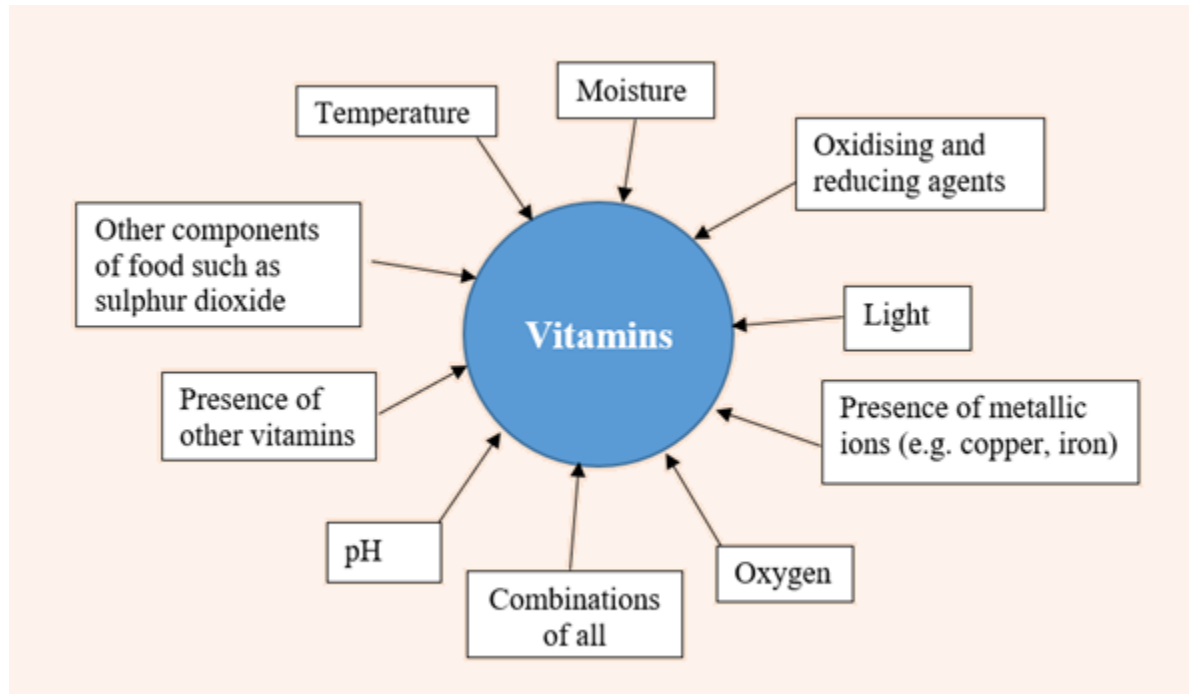


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2 Figure 1. Schematic diagram of a complex coacervation encapsulation process. Recreated based on Ghosh (2006), Thies (2003) and Kim, Yang,  
3 Park, Lim, and Cha (2017)

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7 Figure 2. Main factors affecting vitamins' stability

1    Table 1. Wall materials commonly used for microencapsulation in the food industry

	Physical Property	Animal	Plant	Marine	Microbial	Synthetic/mineral
Carbohydrate	hydrophobic	Chitosan	Starch	Carrageenan	Xanthan gum	Cyclodextrin
			Glucose syrup	Agar	Gellan	Octenyl succinate starch
			Cellulose extracts	Alginate	Dextran	
			Guar gum		Curdlan	
			Pectin		Pullulan	
			Galactomannans			
			Soluble soy polysaccharides			
			Maltodextrins			
			Arabic gum			
			Karaya gum			
			Tragacanth gum			
Protein	hydrophobic	Gelatin	Gluten			
		Casein	Soy			
		Whey	Pea			
		Egg White	Rice			
		Lactoglobulin	Sorghum			
		Caseinate	Lupine			
			Zein			

<b>Lipid</b>	hydrophilic	Fat	Fat/oil	Ethyl cellulose
		Fatty acids	Fatty acids	Sorbitan esters
		Glycerides	Glycerides	Hydrogenated fat
		Phospholipids	Phospholipids	Paraffin Wax
		Beeswax	Plant sterols	Microcrystalline wax
		Shellac	Carnauba wax	
<b>Polymers</b>	hydrophobic			Polyethylene glycol
				Polyvinyl acetate
				Polyvinyl pyrrolidone

2 Modified based on Wandrey et al. (2010), Sobel et al. (2014), Javier D. Hoyos-Leyva et al. (2018), and Reineccius (2019)



3 Table 2. A summary of vitamin microencapsulation methods, wall material, encapsulation efficiency (EE), particle size, and release and  
4 retention from recent studies in food science

Core particle	Method	Wall materials	EE (%)	Particle size	Release and Retention notes	Source
Ascorbic acid	Spray drying	Taro starch	20.9	14.5 µm	Degradation rate was 0.006 at 13% RH and 0.029 at 72% RH at 55°C	(J. D. Hoyos-Leyva et al., 2018)
Ascorbic acid	W/O/W double emulsion	Sugar-free rebaudioside-sweetened model beverage	86.5 -95	0.46- 0.80 µm	Higher entrapment efficiency, storage stability and improved chemical stability than single emulsion. 70.02-79.97% retention efficiency after 30 days Heat treatment at 80°C reduced the retention efficiency	(Kheynoor, Hosseini, Yousefi, Hashemi Gahruie, & Mesbahi, 2018)
Ascorbic acid and Folic acid	Liposome entrapment	Soybean phosphatidylcholine, cholesterol, chitosan, Tween 80	AA: 34.63- 80.96 FA: 64.25- 87.41	138.58 - 249 nm	Hydroxyl radical scavenging activity-44.83- 57.15% Improved retention after 40 days storage- AA: 20.43-25.59% FA: 28.17-33.42% Control- 0.13-0.32%	(Jiao et al., 2018)

					Chitosan enhanced stability, encapsulation efficiency and antioxidant activity	
Ascorbic acid	Spray drying	Chitosan, modified chitosan and sodium alginate	Not tested	3 µm	43.6%- 45.4% yield	(Jiao et al., 2018)
					Chitosan coating resulted in the highest yield and protection with release time 120 min.	
Ascorbic acid	Spray drying	Chitosan, tripolyphosphate cross-linking agent	45.05-58.30	6.1-9.0 µm	Crosslinked chitosan improved the efficiency of encapsulation	(K. G. H. Desai & Park, 2005)
					High stability of ascorbic acid observed	
					The increased concentration of crosslinking agent decreased encapsulation efficiency	
Ascorbic acid	Liposome	Soy phosphatidylcholine, stearic acid, calcium stearate	85.31-86.33	0.5-400 µm	Protective effect of vitamin C in orange juice from pasteurisation (65°C for 30 min) was found.	(Marsanasco et al., 2011)
Ascorbic acid	Thermal phase separation (TPS)	Ethyl cellulose, coacervation-inducing agent	TPS-NA	TPS 16.9-61.9 µm	Protection from oxidation, no colour change after one month storage	(M. S. Uddin, 2001)
	Melt dispersion (MED)	Carnauba wax	MED- NA	MED ~50 mm	Carnauba wax and β-cyclodextrin were effective coating material	

	Solvent evaporation (SE)	Ethyl cellulose, plasticizer (triethyl citrate)	SE- NA	SE NA	with higher encapsulation efficiency and stabilisation of acid	
	Spray drying (SD)	gel, starch, ethyl cellulose, - cyclodextrin,	SD- below 50	SD 90-280 $\mu\text{m}$		
$\beta$ -Carotene	Spray drying	N-octenyl succinate anhydride modified starches (HI-CAP, CAPSUL and CAPSUL TA)	Not tested	118-159 nm	Retention after 30 days: 71.87% at RH 11% and 58.04% at RH 97% The relation between oxygen permeability of the matrixes and vitamin degradation was found.	(Liang et al., 2013)
$\beta$ -Carotene (Piquillo pepper extract)	Emulsion-spray drying	Gum arabic	77.1	5.46 $\mu\text{m}$	$\beta$ -Carotene were stable when entrapped in 35 days storage at room temperature. No other storage conditions were given.	(Romo-Hualde, Yetano-Cunchillos, González-Ferrero, Sáiz-Abajo, & González-Navarro,

2012)

Retinol	Liposome entrapment	Combination of phosphatidylcholine and cholesterol	94.52- 99.31	31.7-41.42 $\mu\text{m}$	After 10 days of storage- 90% at pH 7, 87% at pH 9, and 39.46% at pH 5	(S. C. Lee et al., 2005)
Folic acid	Impregnation method (Pérez-Esteve et al., 2015)	Inorganic gated mesoporous silica particles (calcinated MCM-41)	75	862 $\pm$ 59 nm	Higher stability facilitating target release, protection from photodegradation, thermostability, high retention (84–94.5%) after 28 days of storage.	(Ruiz-Rico et al., 2017)
Folic acid	Spray drying	Horse chestnut starch and $\beta$ -cyclodextrin	Starch (SF)- 57.29 $\beta$ -cyclodextrin (BF)- 76.10	SF 28.26-227.3 $\mu\text{m}$ BF 30.09-145.9 $\mu\text{m}$	Protection from environmental factors ensuring release in the GI tract. Potential of horse chestnut starch in stabilising FA.	(Ahmad et al., 2017)
Folic acid	Spray drying	Rice starch with gum arabia or guar gum or xanthan gum or $\kappa$ -carrageenan	65-85	15-45 $\mu\text{m}$	Thermostability, higher retention with $\kappa$ -carrageenan and alg-pec, 97% retention after boiling the noodles for 3min 20s - 3min 40s	(Hau, 2008)

		combination of alginate and Low methoxyl pectin							
Folic acid	Electrospinning	Sodium alginate, pectin, polyethylene oxide	Not tested		140-131 nm	Almost 100% retention at controlled light and pH	Higher stability when crosslinked with ethanol	(Alborzi et al., 2013)	
5-methyl tetrahydrofolic acid	Combination of spray drying and extrusion	Combination of pectin and alginate	spray drying- 60 Extrusion- not tested			84-94.5% retention after thermal treatment (boiling/autoclaving)		(Shrestha et al., 2012)	
Folic acid	Extrusion	alginate, pectin, xanthan gum, gelatine, iota-carrageenan in a single form or combination	55-89		Not tested	Alg-pec coating significantly enhanced the stability and pressure tolerance properties		(Madziva et al., 2005, 2006)	
Pantothenic acid	Liposome and Extrusion	Phospholipon 90 G, alginate, pectin	Liposome- 75 Extrusion- 60		Liposome- 100-240 nm Extrusion- 240-300 µm	After 14 days of storage, only 20% release occurred at pH 4	Thermostable capsules formed No further effect of alginate-pectin was noted	(Ota et al., 2018)	
Thiamine	Liposome	Phosphatidylcholine	97		108-1351 nm	Stability/retention was not tested. Chloroform was used to dissolve phosphatidylcholine, therefore not suitable for human		(Juveriya Fathima et al., 2016)	

						consumption	
Riboflavin	Cold-set gelation and Immobilisation	Whey protein isolate	24.5-57	Not tested		Fast release of riboflavin, no or little protection Controlling diffusional losses is required to make use of this carrier Release rate increased with the decreased hydrophobicity of the active	(O'Neill, Egan, Jacquier, O'Sullivan, & Dolores O'Riordan, 2014, 2015)
Riboflavin	Spray drying	Gum Arabic, $\beta$ -Carotene	Not tested	Not tested		20% photo protection Gum arabia alone or with $\beta$ -carotene can protect the self-photoinduced degradation of RF, but with $\beta$ -carotene is more efficient	(Boiero et al., 2014)
Vitamin B <sub>12</sub>	Coextrusion	Rice flour, guar gum, xanthan gum, carboxymethyl cellulose	Not tested	Not tested		Best retention (77%) of vitamin B12 achieved at 140°C/150 rpm/4 kg/h extrusion parameters Carboxymethyl cellulose enhanced physico-functional properties	(Bajaj & Singhal, 2019)

Vitamin B <sub>12</sub>	Spray drying	chitosan, modified chitosan and sodium alginate	Not tested	Not tested	41.8%- 55.6% yield Chitosan coating resulted in the highest yield and protection with release time 120 min but rough surface	(Estevinho, Carlan, Blaga, & Rocha, 2016)
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# \*Graphical Abstract

